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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/813,331	03/29/2004	Bill J. Peck	10031531-1	5115

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EXAMINER	
WILDER, CYNTHIA B	

ART UNIT	PAPER NUMBER
1637	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/813,331	PECK ET AL.	
	Examiner	Art Unit	
	Cynthia B. Wilder, Ph.D.	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 March 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-24 and 26-28* is/are pending in the application.

4a) Of the above claim(s) *17-24,26 and 27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 2, 4-16 and 28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

FINAL ACTION

1. Applicant's amendment filed 3/13/2007 is acknowledged and has been entered. Claims 1 and 4 have been amended. Claims 3 and 25 have been canceled. Claim 28 has been added. Claims 17-24 and 26-27 are withdrawn from consideration as being drawn to a non-elected invention. Claims 1, 2 and 4-16 and 28 are pending and discussed in the instant Office action. All of the arguments have been thoroughly reviewed and considered but are deemed moot in view of the new grounds of rejections necessitated by Applicant's amendment of the claims. Any rejection not reiterated in this action has been withdrawn as being obviated by the amendment of the claims.

This action is made FINAL.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Previous Rejections

3. The prior art rejection under 35 USC 102(b) as being anticipated by Anderson et al is withdrawn in view of Applicant's amendment. The prior art rejection under 35 USC 35 USC 103(a) as being unpatentable over Anderson et al or Anderson in view of Blanchard et al is withdrawn in view of Applicant's amendment of the claims. The double patenting rejection is withdrawn in view of Applicant's submission of a proper terminal disclaimer 37 CFR 3.73(b).

New Ground(s) of Rejections

THE NEW GROUND(S) OF REJECTIONS WERE NECESSITATED BY APPLICANT'S AMENDMENT OF THE CLAIMS:

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 1, 2, 4-15 and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Anderson et al (citation made of record in previous office action) in view of in view of Schleifer (A) {U.S. Patent No. 6,077,674, issued 20 June 2000) or Schleifer (B) (U.S. Patent No. 6,309,828, issued 30 October 2001).

Regarding claims 1, Anderson et al disclose the method comprising contacting a blocked monomer at first and second locations having functional groups (e.g. cpg supports having the first monomer attached, Column 19, lines 55-58) under conditions sufficient for the monomer to covalently bond to the surface. Anderson et al further teach detritylation of the nucleotide with a blocking fluid; namely, step (i) of Table I (column 20), which generates an unblocked attached nucleoside nucleotide. Anderson et al further teach displacing the deblocking fluid with a purging fluid; namely, the solid supports are exposed to reagents sequentially wherein the reagents are kept separate based on density (column 5, lines 3-38 and column 6, lines 13-36) forming a liquid-liquid interface such that the solid support is not exposed to a triple phase interface (column

12, lines 28-67 and Fig. 2A-2D). Anderson et al also teach the reacting of the unblocked attached nucleotide with another blocked nucleoside monomer; namely, coupling step ii of Table I (column 20); removing blocking groups to generate a function group and reiterating the steps to produce the array of at least two ligands (Column 19, line 55-Column 20, line 50). Anderson et al further teach the method wherein the solid supports are exposed to reagents sequentially wherein the reagents are kept separate based on density (Column 5, lines 3-38 and Column 6, lines 13-36) forming a liquid-liquid interface such that the solid support is not exposed to a triple phase interface (Column 12, lines 28-67 and Fig. 2A-2D).

While the reference does not use the term "array", the term is defined by dictionary.reference.com as "a larger group, number or quantity of people or things". Anderson et al teach production of a plurality of oligonucleotides attached to cpg substrate ("1. Oligonucleotide Synthesis", Columns 19-22 and Column 24, lines 5-35). Anderson et al further teach wherein the polymers are cleaved from the support for subsequent use and/or immobilization (col. 14 and col. 20, lines 10-25, e.g., hybridization to oligonucleotides immobilized on solid supports (col. 20, lines 20-21). While this teaching suggest that the polymers are subsequently immobilized, Anderson et al do not expressly teach the production of addressable array. However, polymer synthesis on cpg supports followed by polymer cleavage for the production of an addressable array was well known and routinely practice in the art at the time the claimed invention was made as taught by Schleifer (A) and (B).

In a method similar to that of Anderson et al, Schleifer (A) teaches method steps of polymer synthesis comprising repeated monomer additions to cpg supports (col. 9, lines 6-10), cleavage of the polymers from the supports (col. 10, lines 10-15) and immobilization of the polymers to feature locations on the array (col. 10, lines 37-42) whereby "costly and time consuming purification steps" is avoided while providing a high purity full length oligonucleotide array (col. 10, lines 47-51).

Schleifer (B) teaches a similar method of polymer synthesis comprising repeated monomer additions to cpg supports, cleavage of the polymers from the supports and immobilization of the polymers to feature locations on the array (col. 9, line 22 to col. 10, line 30 and Example 3) whereby an addressable array is produced (see definition of an array, col. 1, lines 13-15). Schleifer (B) teaches this polymer synthesis coupled to array production is an efficient, cost effective method of spatially integrating polymer synthesis and replicate array fabrication (abstract and col. 2, lines 22-31).

It would have been obvious to one or ordinary skill in the art at the time the claimed invention was made to apply the polymers synthesized by Anderson et al to the further step of addressable array fabrication taught by Schleifer (A) and/or (B). One of ordinary skill in the art at the time of the claimed invention would have been motivated to do so based on the well known practice of addressable immobilization of pre synthesized polymers as taught by Schleifer (A) and (B). One of ordinary skill in the art would have been further motivated to do for the expected benefits of producing replicate arrays via efficient cost-effective methods of spatially integrating polymer synthesis and array fabrication as suggested by Schleifer (B) (abstract, col. 2, lines 22-31) and for the

further benefits of providing high purity full-length oligonucleotides while avoiding costly and time consuming purification steps as suggested by Schleifer (A) (col. 10, lines 47-51).

Alternatively, it would have been obvious to one of ordinary skill in the art at the time of the claimed invention was made to apply the deblocking fluid synthesis steps of Anderson et al to the polymer synthesis of either Schleifer (A) or (B). Anderson et al teach polymer synthesis in particulate beds is problematic in that fluid flows through the bed is non-uniform resulting in non-uniform reactions and hence inefficient and inaccurate polymer synthesis (col. 1-4). Anderson et al further teach that their method of precise fluid control through the particle bed minimizes the problems of micro- and macro-anomalous flow provides precise and efficient polymer synthesis (col. 5 and 6). Therefore, one of ordinary skill in the art at the time of the claimed invention would have been motivated to apply the precisely controlled fluid flow of Anderson et al to the particle bed synthesis of Schleifer (A) and/or (B) for the expected benefit of precise and efficient polymer synthesis while eliminating the problems inherent in particle bed synthesis as taught by Anderson et al (col. 1-6).

Regarding Claims 2 and 3, Anderson et al disclose the method wherein the sequentially applied liquids have a different density greater than zero (i.e. increasing density, Column 6, line 57-Column 7, line 14).

Regarding claims 4, Anderson et al wherein the washing fluid has a density that is lower than the density of the deblocking fluid (Column 5, lines 3-38 and Column 6, lines 13-36). In one embodiment, Anderson et al teach the deblocking (detritylation)

fluid has a density that is greater than that of methylene chloride (i.e., 1.325 g/mL; column 21, lines 1-10). Detritylation is followed with a wash using acetonitrile, which has a density of 0.714 g/mL (Table II, step 3). Calculating the density difference using pure methyl chloride results in an Atwood number of 0.2996; a higher density deblocking fluid gives a higher Atwood number.

Regarding Claim 5, Anderson et al disclose wherein the wash is a low viscosity (see col. 7, lines 68 to col. 8, line 1 and Table II, step 3 with discloses that the wash solution is acetonitrile).

Regarding claim 6 and 8, Anderson et al discloses wherein the wash fluid is acetronitrile (column 13, line 67-column 14, line 1), which has a low viscosity (col. 7, line 68 to col. 8, line 1). It is commonly known in the art base standard physical data that acetonitrile has a viscosity of 0.38 cp. Therefore, it is an inherent property that the wash fluid (acetonitrile) has a viscosity that does not exceed about 1.2 cP.

Regarding claim 7, Anderson et al disclose wherein said wash fluid is an organic fluid (Table II, step 3).

Regarding Claim 9, Anderson et al disclose the method wherein displacing comprises flowing the subsequent liquid across the surface to produce a stratified liquid interface that moves across the surface (Column 12, lines 28-67 and Fig. 2A-2D).

Regarding Claim 10, Anderson et al disclose a method of producing an array of at least two different polymeric ligands (e.g. oligonucleotides synthesized on control pore glass, the two different sequences being e.g. product and failed sequences, Column 20, lines 10-25) as previously discussed above. Anderson et al further teach

the method wherein the steps are performed in a flow cell wherein the flow rate is controlled and monitored during passage of reagents (Column 5,lines 25-27; Column 14, lines 44-53 21). Anderson et al teach that it is important to control the flow rate because some synthesis steps take more or less time than other steps and because reagent waste resulting from excess use of reagents is expensive (Column 21, lines 30-65) but they are silent regarding specific flow rates. However, the reference clearly suggests that the flow rate is adjusted to maximize reagents and synthetic step. Therefore, It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to adjust the flow rate during the synthesis steps of Anderson to obtain optimal flow rates (e.g. about 1-20 cm/x). One of ordinary skill in the art would have been motivated to adjust the flow rate so as to maximize syntheses reaction with minimal waste of reagents as desired by Anderson et al (Column 21, lines 30-65).

Regarding Claim 11, Anderson et al teach wherein the method comprises a sensing movement (rotation) that moves a stratified interface across the surface (column 12, lines 28-67 and Fig. 2A-2D).

Regarding Claim 12-14, Anderson et al disclose the method wherein the steps are preformed in a flow cell i.e. internal space for fluid flow so as to contact solid support (Column 5, lines 20-38).

Regarding Claim 15, Anderson et al disclose the method wherein said surface is contacted with a capping liquid prior to said deblocking (Column 13, line 59-Column 14, line 11 and Column 19, line 55-Column 20, line 50).

Regarding claim 28, Anderson et al teach wherein the substrate is a planar substrate, e.g., flat disc (col. 6, lines 49-52).

Therefore, Anderson et al meets the limitation of the claims noted above.

Claim Rejections - 35 USC § 103

6. Claim 16 is rejected under 35 U.S.C. 103(a) as being unpatentable over Anderson et al Schleifer (A) and Schleifer (b) and further in view of Blanchard (citation made of record in prior Office Action).

Regarding Claim 16, Anderson et al in view of Schleifer (A) and Schleifer (B) disclose the method of claim 1 further comprising contacting a blocked monomer at first and second locations having functional groups (e.g. supports having the first monomer attached, (see Anderson, column 19, lines 55-58) under conditions sufficient for the monomer to covalently bond to the surface as previously discussed above.

Anderson et al in view of Schleifer (A) and Schleifer (B) do not teach monomers addition using a pulse-jet.

However, pulse-jet addition of monomers during multi-step synthesis of polymers was well known in the art at the time the claimed invention was made as taught by Blanchard.

Blanchard teaches a similar method of oligonucleotide synthesis on a solid support wherein the support is placed in a flow cell for all reaction except for monomer addition (Column 4, lines 3-22). Blanchard teach the monomer addition using a pulse jet provides precise, discrete and small volumes of monomer are added to a support

(Column 5, lines 41-56) whereby multiple and different monomers dispensed simultaneously thereby greatly reducing the time of array synthesis (Column 11, lines 48-61).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the pulse-jet dispenser of Blanchard to the monomer addition step of Anderson et al. One of ordinary skill in the art would have been motivated to do so for the expected benefit of simultaneously providing multiple and different monomers precisely at, discrete and small locations on to the support (e.g. membrane/disc) of Anderson et al with greatly reduced time of array synthesis as taught by Blanchard (Column 5, lines 41-56 and Column 11, lines 48-61).

Conclusion

7. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia B. Wilder, Ph.D. whose telephone number is (571) 272-0791. The examiner can normally be reached on a flexible schedule.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Cynthia B. Wilder, Ph.D.
Patent Examiner
Art Unit 1637

KENNETH R. HORLICK, PH.D
PRIMARY EXAMINER

5/24/07